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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/660,862 09/13/00 POLLACK

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EXAMINER

024201 HM12/1102
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FORD, V	
ART UNIT	PAPER NUMBER

1645

DATE MAILED: 11/02/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/660,862

Applicant(s)

POLLACK, WILLIAM

Examiner

Vanessa L. Ford

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 5-13 is/are pending in the application.
- 4a) Of the above claim(s) 10-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 5-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

FINAL ACTION

1. This Office Action is responsive to Applicant's response in paper No. 6 to the first Office Action in paper No. 4. In response to the Amendment filed August 22, 2001, claim 1 has been amended. Claims 2-4 have been cancelled. Claims 5-13 have been newly added. Claims 1 and 5-13 are pending.

2. ***Election/Restriction***

Newly submitted claims 10-13 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons:

Newly submitted claims 10-12, drawn to a method of treating a patient envenomated by the sting of an insect comprising administering a composition comprising IgG4 essentially free of other IgG subtypes to a patient envenomated by an insect sting and claim 13, drawn to a pharmaceutical composition. Claims 10-12 and 13 are distinct from examined claims 1-4, drawn to a method of manufacturing IgG immune globulin, since claims 1-4 are drawn to a method of making, whereas claims 10-12 are drawn to a method of using and claim 13 is drawn to a product. Claims 1-4 and claims 10-12 are drawn to different methods, which comprise different method steps, parameters and endpoints. Claims 1-4 and claim 13 are related as product and process of making. The pharmaceutical composition can be used to treat bacterial infections. Furthermore, the classification for the pharmaceutical composition is class 530, subclass 387.1, the classification for the method of treating a patient envenomated by

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the sting of an insect comprising administering a composition comprising IgG4 essentially free of other IgG subtypes to a patient envenomated by an insect sting is classified in class 424, subclass 130.1, while the classification for a method of manufacturing IgG immune globulin is class 435, subclass 69.6. Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 10-13 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Applicant's arguments with respect to claims 1-4 have been considered but are moot in view of the new ground(s) of rejection.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 1 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites "essentially free". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "essentially free" cannot be ascertained. Clarification as to the meaning of this term is required.

5. Claim 5 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites "immune donor". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "immune donor" cannot be ascertained. Clarification as to the meaning of this term is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1 is being rejected under 35 U.S.C. 102(b) as being anticipated by Zolton et al (*U.S. Patent 4,597,966 published July 1, 1986*).

Claim 1 is drawn to a method of manufacturing an IgG4 immunoglobulin that comprises the steps of adjusting the plasma to a pH of about 6.5 and a conductivity of between 3.5 and 6 millisiemens, contacting the plasma obtained from step (a) with an anion exchange resin to obtain an anion exchange effluent and contacting the effluent of step (b) with a cation exchange resin to obtain a cation exchange effluent that comprises IgG4 essentially free of other IgG subtypes.

Zolton et al teach a method of preparing a stabilized highly purified immunoglobulin preparation that comprises a raw immunoglobulin obtained from a

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sterilized human donor pool which has been frozen individually, thawed, pooled (example 1, column 6, lines 56-68), concentrated by ultrafiltration (example 4, column 7, lines 58-61), L histidine and glycine added to stabilize the raw immunoglobulin solution (column 7, lines 64-68 and column 8, line 1-7), filtered and lyophilized (example 6, column 8, lines 13-21), the concentrated raw immunoglobulin was washed with 0.023M (i.e. the instant "about 0.03M") sodium chloride buffer prior to ion exchange chromatography (column 7, lines 5-9), pH adjusted to about 6.4 and conductivity adjusted to about 2.7 millisiemens (example 5, column 8 lines 4-7) and the concentration of the immunoglobulin solution is 5 percent or less more preferably about 0.05 to 5 weight percent and most preferably 1 to about 2 weight percent (column 4, lines 38-41). It would be inherent that the immunoglobulin prepared by the method of preparing a stabilized highly purified immunoglobulin preparation of Zolton et al would comprise IgG4 and be essentially free of other IgG subtypes. Zolton et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zolton in view of Cheung et al, (*Annals of Allergy, Volume 50, March 1983, p. 155-160*).

Zolton et al teaches a method of preparing a stabilized highly purified immunoglobulin preparation that comprises a raw immunoglobulin obtained from a sterilized human donor pool which has been frozen individually, thawed, pooled (example 1, column 6, lines 56-68), concentrated by ultrafiltration (example 4, column 7, lines 58-61), L histidine and glycine added to stabilize the raw immunoglobulin solution (column 7, lines 64-68 and column 8, line 1-7), filtered and lyophilized (example 6, column 8, lines 13-21), the concentrated raw immunoglobulin was washed with 0.023M (i.e. the instant "about 0.03M") sodium chloride buffer prior to ion exchange chromatography (column 7, lines 5-9), pH adjusted to about 6.4 and conductivity adjusted to about 2.7 millisiemens (example 5, column 8 lines 4-7) and the concentration of the immunoglobulin solution is 5 percent or less more preferably about 0.05 to 5 weight percent and most preferably 1 to about 2 weight percent (column 4, lines 38-41).

Zolton et al do not teach immune donors.

Cheung et al teach sera obtained from beekeeper's and honey bee sting allergic patients on immunotherapy. Cheung et al teach that most of the beekeepers had been sting by a bee within the year prior to the study. Cheung et al teach that none of the beekeepers had anaphylactic reactions to bee stings nor were any stung under controlled conditions (page 156, paragraph 4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to obtain the sera used in the method of preparing a stabilized highly purified immunoglobulin preparation as taught by Zolton et al from the immune donors (beekeepers) as taught by Cheung et al because Cheung et al teach that beekeepers that have frequent exposure to bee stings have few clinically significant reactions, have distinctly high honey bee venom (HBV) IgG levels and the association of high HBV IgG4 with beekeepers might suggest a biological role of HBV IgG4 in the protection against anaphylactic reactions or as a laboratory marker of protection (page 158, last paragraph and page 159, first column).

8. Claims 1 and 6⁷ are rejected under 35 U.S.C. 103(a) as being unpatentable over Zolton in view of Sirna (*U.S. Patent No. 5,908, 827, published June 1, 1999*).

Claims 1 and 6-7 are drawn to a method of manufacturing the immune globulin of claim 1 wherein the said anion exchange resin is a DEAE Sepharose® and the cation exchange resin is a CM- Sepharose®.

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Zolton et al teach a method of preparing a stabilized highly purified immunoglobulin preparation that comprises a raw immunoglobulin obtained from a sterilized human donor pool which has been frozen individually, thawed, pooled (example 1, column 6, lines 56-68), concentrated by ultrafiltration (example 4, column 7, lines 58-61), L histidine and glycine added to stabilize the raw immunoglobulin solution (column 7, lines 64-68 and column 8, line 1-7), filtered and lyophilized (example 6, column 8, lines 13-21), the concentrated raw immunoglobulin was washed with 0.023M (i.e. the instant "about 0.03M") sodium chloride buffer prior to ion exchange chromatography (column 7, lines 5-9), pH adjusted to about 6.4 and conductivity adjusted to about 2.7 millisiemens (example 5, column 8 lines 4-7) and the concentration of the immunoglobulin solution is 5 percent or less more preferably about 0.05 to 5 weight percent and most preferably 1 to about 2 weight percent (column 4, lines 38-41).

Zolton et al do not teach the use of a DEAE Sepharose® and a CM- Sepharose®.

Sirna teaches the use of a DEAE Sepharose® and a CM- Sepharose® used in an extraction and purification process by ion-exchange chromatography and high resolution chromatography (see the Abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use a DEAE Sepharose® and a CM-Sepharose® in the method of preparing a stabilized highly purified immunoglobulin preparation as taught by Zolton et al because Sirna demonstrates that the isolation of a raw fraction or protein during extraction and purification can be performed using a DEAE Sepharose® and a

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CM- Sepharose® through ion exchange chromatography and high resolution chromatography (column 2).

9. Claims 1, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zolton et al in view of Thomas (*U.S. Patent No. 4,089,944, published May 16, 1978*).

Claims 1, 8 and 9 are drawn to a method of claim 1 further comprising the steps of adding NaCl to the final concentration of 0.03 to 0.05 M NaCl, filtering the solution, centrifuging the filtrate, freezing the supernatant, thawing the frozen supernatant, adding lactose to the thawed supernatant to a final osmolarity of between 0.22 to 0.35 OsM, filtering the solution, freezing the filtered solution, thawing the frozen solution and lyophilizing the solution.

Claims 1, 8 and 9 are drawn to a method of manufacturing an IgG4 immunoglobulin that comprises the steps of adjusting the plasma to a pH of about 6.5 and a conductivity of between 3.5 and 6 millisiemens, contacting the plasma obtained from step (a) with an anion exchange resin to obtain an anion exchange effluent and contacting the effluent of step (b) with a cation exchange resin to obtain a cation exchange effluent that comprises IgG4 essentially free of other IgG subtypes.

Zolton et al teaches a method of preparing a stabilized highly purified immunoglobulin preparation that comprises a raw immunoglobulin obtained from a sterilized human donor pool which has been frozen individually, thawed, pooled (example 1, column 6, lines 56-68), concentrated by ultrafiltration (example 4, column 7,

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lines 58-61), L histidine and glycine added to stabilize the raw immunoglobulin solution (column 7, lines 64-68 and column 8, line 1-7), filtered and lyophilized (example 6, column 8, lines 13-21), the concentrated raw immunoglobulin was washed with 0.023M (i.e. the instant "about 0.03M") sodium chloride buffer prior to ion exchange chromatography (column 7, lines 5-9), pH adjusted to about 6.4 and conductivity adjusted to about 2.7 millisiemens (example 5, column 8 lines 4-7) and the concentration of the immunoglobulin solution is 5 percent or less more preferably about 0.05 to 5 weight percent and most preferably 1 to about 2 weight percent (column 4, lines 38-41).

Zolton et al differ by not teaching various freezing and thawing steps and also by not teaching the addition of a monosaccharide or disaccharide to the raw immunoglobulin.

Thomas teaches a rapidly solubilized anti-hemophilic factor (AHF) composition and process for preparing the same. Thomas teaches the addition of disaccharides such as maltose, lactose and sucrose to an AHF composition. Thomas teaches that the addition of disaccharides to the AHF composition can occur at any point during or prior to preparation. Thomas further teaches that the addition of disaccharides enhance the rate of solubility (column 3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the lactose as taught by Thomas to the method of preparing a stabilized highly purified immunoglobulin preparation as taught by Zolton et

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al because Thomas teaches that the addition of monosaccharides enhance the rate of solubility in compositions.

It is well known in the art to freeze and later thaw purified fractions at certain convenient points in the process of antibody purification. This is done to pool large amounts of purified antibody fractions before use or further processing or to store purified antibody fractions to be used at a later date. This is evidenced by Rhodes (*U.S. Patent No. 5,346, 687, published September 13, 1994*) which teaches that frozen purified antibody can be frozen in a vial and maintained for indefinite period before use (claim 5).

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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11. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.


Vanessa L. Ford
Biotechnology Patent Examiner
October 25, 2001


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